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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,014	07/03/2003	Richard A. Earl	102258.156US1	5448
25270	7590	12/30/2004	EXAMINER	
EDWARD D GRIEFF HALE & DORR LLP 1455 PENNSYLVANIA AVE, NW WASHINGTON, DC 20004			SACKY, EBENEZER O	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/612,014

Applicant(s)

EARL ET AL.

Examiner

EBENEZER SACKY

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-58 is/are pending in the application.
- 4a) Of the above claim(s) 5-54 and 56-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☒ Claim(s) 55 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 01/16/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

Claims 1-58 are pending.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

Receipt of the Information Disclosure Statement filed 08/23/04 is acknowledged and has been entered into the file. Signed copies of the 1449 are attached herewith.

Claim objection

Claim 1, page 130, line 23 it appears non-elected substituent Q should be Q' page 135, line 4, "proviso" has been misspelled as ---provio---. Correction is required.

Response to Restriction

Applicant's election with traverse of Group X, species of Example 20, (N-methyl-N-(((2-nitrooxy) ethyl) oxycarbonyl) methyl) carbamoyl) methyl (2S)-2-(6-methoxy (2-naphthyl) propanoate in the reply filed on 10/27/04 is acknowledged. However, further restriction is required based on the numerous choices for example "X" which are variously classified and raise different issues of patentability based at the very least on

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WO '499' which is pertinent to subject matter similar to excluded RN 410071-57-7 having X as choice (17). Also see WO '249' which is pertinent to subject matter similar to excluded RN number 311336-65-9 having X as choice (26).

Xa. Claims 1-4, drawn to compounds and compositions where X is choices 1 and 2.

Xb. Claims 1-4, drawn to compounds and compositions where X is choice (3) and 17 where Q' is piperazine link.

Xc. Claims 1-4, drawn to compounds and compositions where X is choices 4, 5, 7-9, 14, 27-28 and 32-33.

Xd. Claims 1-4, drawn to compounds and compositions where X is choices 21 and 42.

Xe. Claims 1-4, drawn to compounds and composition where X is Q' containing links not provided for by (Xb) namely, choices 13, 16-18, 20, 22-25, 30-31, 34-40, 43 and 44.

Xf. Claims 1-4, drawn to compounds and compositions where X is choices 6, 19 and 26.

Xg. Claims 1-4, drawn to compounds and compositions where X is choices 10-12, 15 and 41.

Applicants' elected species falls within Group Xc above which has been only searched by the Examiner. Applicants are advised that the claims will only be examined with respect to Group Xc subject matter.

The wide disparity among the various subgroups requires that many divergent fields must be searched, including but not limited to heterocyclic classes 540, 544, 546, 548, 549 etc, non-heterocyclic classes 560, 564, 568 etc. Thus, the vast number of theoretically conceivable compounds comprised under formulae (I) of claim 1 constitutes an undue burden on the Examiner. Differing issues of patentability exist based on the many provisos excluding compounds already known in the prior art which are closer in structure to some of the compounds within instant claims than they in turn are to each other.

The following corrective action have been taken with regards to the restriction requirement mailed on 09/03/04:

1. Applicants indication with regards to typographical error in XII is correct. Formula 12 should have been formula 14. Thus, Group XII is formulae 14, 39 and 49.
2. Group XIV is incorrect. Hence, Group XIV is limited to formulae 16, 20 and 25.
3. Group V is directed to compounds of formula (I) wherein R_n is formula 5. Formulae 29, 33 and 45 remains with Group XVIII.
4. Group XX has been eliminated since formulae 41 and 51 have already been grouped with Group IV.
5. Formula 14, which has not yet been assigned to any group will be grouped with Group XII. Therefore, Group XII becomes formulae 14, 39 and 49.

6. Formula 17, which has not yet been assigned will be grouped with Group II. Therefore, Group II becomes 2, 17, 22, 27 and 38. The number of Groups has reduced to 56.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification is not adequately enabled for the scope of nitrosated compounds elected which can contain a variety of linking chains and rings (see R_4/R_4' as well as R_j in T). There is no sufficient enabling disclosure by way of working examples or reasonable disclosure leading to the preparation of such compounds. Compounds made are compounds where R_4 , R_4' and R_j are hydrogen or alkyl groups. No example(s) to any heterocyclic or cycloalkyl compounds have been made. There is no reasonable basis for assuming that the myriad of compounds enumerated by the claim will all share the same physiological properties since they are so dissimilar as to be chemically non-equivalent and there is no basis in the prior art for

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assuming the same. The homogeneity of the 4 examples would provide no insight into structure-activity trends that need to be evaluated. Receptor binding is known to be structure-sensitive in general. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency for Markush group where as herein no examples of diverse nature have been made showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also the factors to be considered in making an enablement rejection have been summarized in *In re Wands* cited in MPEP 2164.01(a), May 2004 edition, which includes factors such as:

1) Breadth of the claims- the claims cover considerable amount of compounds as pointed out above;

2) Level of unpredictability in the art-the invention is pharmaceutical in nature involving the inhibition of cyclooxygenase enzyme. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See *In re Fisher*, 166 USPQ 18;

3) Direction or guidance –as stated above the only compounds actually made are much closer to each other than to remaining scope.

In view of the above considerations the rejection is being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of registry numbers being excluded renders entire scope of claims indefinite. The purpose of 112 second, paragraph is to positively recite what applicants invention is, not what it isn't. The claims are of unclear scope since it recites what is excluded and thus does not clearly define what is within applicants' invention. As stated in *In re Schechter* 98 USPQ 144 such limitations in a claim renders it indefinite "since applicant sought to claim what was not invented, rather than "particularly and distinctly pointing out" what was invented. At the very least what if ACS decides to change and assign new registry numbers to the millions of compounds in their database? Then the registry numbers in the patent becomes meaningless. Further exacerbating the intended scope is the presence of compounds excluded that do not appear to be generically embraced. See for example, the 1st registry number excluded which does not appear to be within the ambit of the claims.

2. In claim 3, it is not clear if applicants are claiming 1 or 2 or 3 nitrosated compounds. Note claim 1 permits one or more ONO_2 groups within X choices. With further regard to claim 3, structural makeup is not readily ascertainable based on naming employing non-IUPAC nomenclature. Applicants are requested to indicate which of these compounds are directed to elected invention.

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WO 02/092072 A2 and WO 03/013499 A2 are cited to show the state of the art.

The cited publications are devoid of the X linking choices of the elected invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (571) 272-0704.

The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is

(703) 308-1235.

EOS

December 27, 2004



EMILY BERNHARDT
PRIMARY EXAMINER

GROUP 120 1000